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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,094	03/27/2001	Richard I. Weiner	UCSF-018/02US	6968

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	PAPER NUMBER
1646	16

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/819,094	Applicant(s) Weiner et al.
	Examiner Michael Brannock	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 3, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *28* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *28* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application: Claims and Amendments

1. Applicant is notified that the amendments put forth in Paper 15, 3/3/03 have been entered in full.

2. Claim 28 is pending.

Oath/Declaration

3. The oath or declaration is defective, as set forth previously. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration, e.g. the correction of Frauke Bentzien's address has not been initialed and dated. See 37 CFR 1.52(c).

Applicant argues that the inventor's signature appears over the changes, thus indicating that the inventor signed the Declaration with the changes. This argument has been fully considered but not deemed persuasive. The examiner admits that he does not understand Applicant's arguments. On viewing the signature of Frauke Bentzien, it would be impossible to determine if the inventor had signed the Declaration before or after the changes had been made. Never-the-

less 37 CFR 1.52(c) requires that alterations to the Declaration must be initialed and dated.

Appropriate action is required.

Response to Amendment

4. Applicant is notified that any outstanding rejections that are not expressly maintained in this Office action have been withdrawn.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 4189426, to Choh Li, 2/1980, in view of US Patent 4853332, to Mark et al., 8/1989.

Li disclose the proteolytic N-terminal fragment of human Placental lactogen, a.k.a. human choriomammotropin (HCS), see col 6. consisting residues 1-133, see col 7. The polypeptide of SEQ ID NO: 18, however, has been mutated to replace the reactive cysteine at position 53 and with serine. The reactive cysteine at this position is well known to be involved in a disulfide bond (e.g. see col 7, line 32 of Li). Li teaches that this reactive cysteine be

neutralized by rendering it incapable of disulfide bond formation by any means known in the art (see col 1, last paragraph to col. 2). Consequently, Li accomplish this by carboxamidomethylation, e.g. col 2 first paragraph. Subsequently, however, Mark et al. disclose an improved method of preventing undesirable disulfide formation at cysteine residues in peptide hormones, e.g. by mutagenically replacing the reactive cysteine residue with a non reactive residue (see col 1), e.g. with serine (e.g. col 5 line 23). Additionally, Li teach that the peptide be present in a pharmaceutically acceptable carrier, e.g. 0.1M tris 8.2 (col 4, L8), i.e. for use in the rat tibia test (Example II).

Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success, to replace the cysteine residue at position 53 of the 16 kDa fragment of human placental lactogen, as taught by Li, with a serine residue as taught by Mark et al.. The motivation to do so is provided by both Li, who teaches that the reactive 53-cysteine be prevented from bond formation, and by Mark et al. who disclose an improved method to accomplish this in peptide hormones (e.g cols 1 and 2).

Applicant's arguments, as they may relate to this rejection, are addressed below. Applicant argues that Li et al. do not disclose the polypeptide of SEQ ID NO: 18. This is true, however, as discussed above, one of ordinary skill in the art would be motivated to produce the polypeptide of SEQ ID NO: 18 following the teachings of Li and Mark. Applicant argues that Li provide no teachings as to the anti-angiogenic properties of the polypeptide. This argument has been fully considered but not deemed persuasive. Such properties would expected to be inherent

to the claimed product, absent evidence to the contrary. Applicant argues that there is no motivation to combine the teachings of the Li and Mark patents to obtain a peptide of SEQ ID NO: 18. This argument has been fully considered but not deemed persuasive. The motivation to do so is provided by both Li, who teaches that the reactive 53-cysteine be prevented from bond formation, and by Mark et al. who disclose an improved method to accomplish this in peptide hormones (e.g cols 1 and 2).

Conclusion

No claims are allowable.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

May 14, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600